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5 procedure-related deaths (0.6%) (4,5). This adverse event rate was similar to that presented by O'Byrne et al. (1): 61 cases of deaths or extracorporeal membrane oxygenation on the day of catheterization (0.96%; n = 6,339). Hence, the authors' statement that "cardiac catheterization in children with PH carries a risk of cardiac arrest of 4.5 to 5.7 per hundred" (1) is incorrect, and the term "catastrophic" adverse outcome is more on the basis of opinion than on facts.

Clearly, we must be aware that the complication rate for cardiac catheterization with or without anesthesia is higher in children than in adults (4,5). Thus, we must weigh the risks and benefits of invasive procedures and perform the latter in experienced PH centers. Nevertheless, we feel strongly that cardiac catheterization with vasodilator testing remains an essential part of the comprehensive PH work-up at diagnosis.

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Please note: Dr. Hansmann is chair and Dr. Apitz is co-chair of the writing group of the Expert Consensus Statement on the Diagnosis and Treatment of Pediatric Pulmonary Hypertension from The European Pediatric Pulmonary Vascular Disease Network (2015). Dr. Hansmann is the American Heart Association co-chair of the writing group of AHA/ATS Joint Guidelines for Pediatric Pulmonary Hypertension (2015); and is a task force member of the 2015 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension.

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To "Cath" or Not in Pediatric Pulmonary Hypertension?

We read with interest the publication of O'Byrne et al. (1) and accompanying editorial by Kreutzer (2) addressing risks associated with heart catheterization (HC) in pediatric pulmonary hypertension (PH). HC is considered crucial in defining diagnosis and prognosis and in guiding treatment strategies. Balancing risks and benefits remains a clinical dilemma. The current study design is flawed by selection of a nonrepresentative, high-risk population of hospitalized children and leaves indications for HC undefined. Diagnoses and complications were on the basis of an administrative registry, a recognized source of error. The observed high risk of the composite endpoint obviously is not representative for the child with PH in general. The risk of catheterization is not consistently adjusted for center volume or experience, and other data from dedicated centers report lower complication rates (3–5). The different complication rates in previous reports could be explained by data from experienced and referral centers for PH, and the current study presentation may now hamper proper discussions on the use of HC. Instead of optimizing an accurate estimate of serious complications of HC, identifying its risk factors and balancing clinical decision making, the current paper will cause a drift away from HC procedures, possibly withholding optimal care. Further, using pulmonary arterial hypertension medications without understanding the pathophysiology may be detrimental, as pulmonary vasodilators can lead to pulmonary edema/worsening ventilation-perfusion matching in certain settings. We support the conclusion of Kreutzer (2) that more accurate outcome assessments are mandatory in large registries within populations of interest, as is the validation of noninvasive tools. Both are aims of the global TOPP (Tracking Outcome and Practice in Pediatric Pulmonary Hypertension)-1 and -2 registries (5).

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REPLY: The Need for Comprehensive Cardiac Catheterization in Children With Pulmonary Hypertension

To "Cath" or Not in Pediatric Pulmonary Hypertension?

We welcome the comments and interest of Drs. Hansmann and Apitz and Dr. Beghetti and colleagues regarding our study. We agree that cardiac catheterization is an essential component of the evaluation of pulmonary hypertension (PH). Our study utilized administrative data from 38 primary children's hospitals in the United States to measure the risk of a catastrophic outcome using a standard definition (1) in children undergoing cardiac catheterization during inpatient and observation admissions. The use of administrative data overcomes the challenge of studying low event rates in a rare condition, and we included more than 6,000 procedures in 4,401 unique patients with a range of risk factors in our analysis. The data from the TOPP (Tracking Outcome and Practice in Pediatric Pulmonary Hypertension) registry were drawn from 31 expert centers in which 908 procedures were performed in 456 patients whose families provided informed consent. As acknowledged by the authors, patients who died may not have been included in the TOPP registry due to the absence of informed consent (2). Our analysis may be more generalizable, because it includes expert and nonexpert centers, many more procedures, and a patient population with a broader range of severity of illness.

The TOPP study and other single-center studies cited in the letter by Drs. Hansmann and Apitz and Dr. Beghetti and colleagues are valuable because they include detailed data from highly experienced pediatric centers with a narrower range of conditions and illness severity. Interestingly, the mortality estimates from these studies are consistent with that from ours. In the series from Beghetti et al. (2), Zuckerman et al. (3), and Bobhate et al. (4), the 95% confidence intervals (CIs) for the observed risks of mortality were 0% to 3.7%, 0.2% to 1.0%, and 0.2% to 1.3%, respectively. The observed risk of mortality within 1 day of catheterization in our study (0.3%; 95% CI: 0.2% to 0.4%) falls within these CIs, suggesting that the study populations and their outcomes are more comparable than implied.

We acknowledge the limitations of administrative data (i.e., reliance on billing codes and missing clinical data); however, our analysis also has several strengths. First, we accounted for the relatedness of procedures within the same individual. A patient who did "well" with the first procedure will be more likely to undergo a second or third procedure, leading to a biased "healthier" population if this relatedness is not considered when analyzing multiple procedures. In TOPP and other studies, every procedure (even if performed on the same patient) was considered independently, which does not fulfill necessary assumptions underlying the analysis (independence of outcomes) and may lead to "over-representation" of lower-risk individuals. Second, our significantly larger study population allowed us to use multivariable analysis to adjust for confounders and provide standardized estimates, which were not calculated in the referenced studies. The estimated risk of a catastrophic adverse outcome for a "standard risk profile" patient (a school-age patient with idiopathic pulmonary hypertension who is not receiving a pulmonary vasodilator and without other risk factors) may be a more useful statistic for comparison than unadjusted observed risk.